

## 90 Human Secreted Proteins

### *Field of the Invention*

This application is a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending United States patent application Serial No: PCT/US98/16235 filed August 4, 1998, which is hereby incorporated by reference, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Applications:

	Filing Date	Appln No.
1.	05-Aug-1997	60/055,386
2.	05-Aug-1997	60/054,807
3.	05-Aug-1997	60/055,312
4.	05-Aug-1997	60/055,309
5.	05-Aug-1997	60/054,798
6.	05-Aug-1997	60/055,310
7.	05-Aug-1997	60/054,806
8.	05-Aug-1997	60/054,809
9.	05-Aug-1997	60/054,804
10.	05-Aug-1997	60/054,803
11.	05-Aug-1997	60/054,808
12.	05-Aug-1997	60/055,311
13.	18-Aug-1997	60/055,986
14.	18-Aug-1997	60/055,970
15.	19-Aug-1997	60/056,563
16.	19-Aug-1997	60/056,557
17.	19-Aug-1997	60/056,731
18.	19-Aug-1997	60/056,365
19.	19-Aug-1997	60/056,367
20.	19-Aug-1997	60/056,370
21.	19-Aug-1997	60/056,364
22.	19-Aug-1997	60/056,366
23.	19-Aug-1997	60/056,732
24.	19-Aug-1997	60/056,371

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and their production.

### *Background of the Invention*

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell

uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoietin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using secreted proteins or the genes that encode them.

### *Summary of the Invention*

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

## *Detailed Description*

### Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

5        In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of  
10       matter, or particular cell is not the original environment of the polynucleotide.

      In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the  
15       extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

      In specific embodiments, the polynucleotides of the invention are less than 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, or 7.5 kb in length. In a further  
20       embodiment, polynucleotides of the invention comprise at least 15 contiguous nucleotides of the coding sequence, but do not comprise all or a portion of any intron. In another embodiment, the nucleic acid comprising the coding sequence does not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene in the genome).

25       As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region,  
30       as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

      In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig  
35       analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As

shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of

5 microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42°

10 C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x-Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the

15 polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a

20 solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH<sub>2</sub>PO<sub>4</sub>; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

25 Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking

30 reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of

35 "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid



molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA  
 5 or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-  
 10 stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and  
 15 RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The  
 20 polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino  
 25 or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result  
 30 from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond  
 35 formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation,

pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W.

- 5 H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

### Polynucleotides and Polypeptides of the Invention

#### 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 1

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: TFKSLWKHWTLAGPGNIGKNWIGR (SEQ ID NO:203). Polynucleotides encoding these polypeptides are also encompassed by the invention.

30 This gene is expressed primarily in bone marrow tissue, and to a lesser extent in eosinophils and fetal liver tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic or immune disorders and diseases, particularly recovery of the hematopoietic system after anticancer therapy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, bone marrow and hemopoietic cells and tissue, eosinophils and other blood cells, hepatic tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone marrow and fetal liver tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the regulation and/or reconstitution of hematopoietic cells after cancer therapy. This gene product is primarily expressed in hematopoietic cells and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoietic lineages. This is particularly supported by the expression of this gene product in fetal liver and bone marrow, the two primary sites of definitive hematopoiesis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:11 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 961 of SEQ ID NO:11, b is an integer of 15 to 975, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 2

When tested against K562 cell lines, supernatants removed from cells containing this gene activated the ISRE (interferon-sensitive responsive element ) pathway. Thus, it is likely that this gene activates kidney cells, and to a lesser extent other cells or cells types, through the JAK-STAT signal transduction pathway. ISRE (interferon-sensitive responsive element ) - also a promoter element found upstream in

many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STATs pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

HEGTWRWEAPTPLQSLGPTTPSLPSVADLCQDGHGGCSEHANCSQVGT (SEQ ID NO:204). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

The protein product of this clone is a homolog of a secreted protein member of the hyaladherin family. It's closest match is TSG-6. The expression of TSG-6 is TNF- and IL-1-inducible, and is found in elevated amounts in synovial fluid from rheumatoid versus normal joints. There is a strong link between the TSG-6 protein and inflammation. The gene was isolated from TNF-induced fibroblasts. It is transcriptionally induced by TNF, LPS, and IL-1. Tissues that express TSG-6 include fibroblasts, monocytes, and synovial cells. It binds hyaluronic acid, as does another member of the CD44 family, which functions as the lymphocyte homing receptor. TSG-6 also complexes with the serpin, inter-alpha-inhibitor (IaI). IaI inhibits proteases such as cathepsin G and leukocyte elastase, which are involved in tissue damage during inflammation. A higher level of TSG-6 protein is found in the synovial fluid of rheumatoid versus normal joints. The most compelling evidence for TSGF-6 as an anti-inflammatory is that it can inhibit IL-1-induced acute inflammation, as well as dexamethasone in the mouse air pouch inflammation model.

This gene is expressed primarily in myeloid progenitor cell line, spleen and bone marrow and to a lesser extent in synovial tissue and adipose tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation caused by acute injury or chronic disease, and other immune system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., inflamed,

immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:108 as residues: Pro-8 to Trp-15, Cys-17 to Asn-36, Leu-42 to Cys-49, Glu-63 to Val-68.

The tissue distribution in immune tissues, in conjunction with the biological activity data, suggests that the protein product of this clone is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

In addition, the expression of this gene product in synovium, as well as the homology to TSG-6, suggests a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial arthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:12 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 2739 of SEQ ID NO:12, b is an integer of 15 to 2753, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.

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### FEATURES OF PROTEIN ENCODED BY GENE NO: 3

When tested against PC12 cell lines, supernatants removed from cells containing this gene activated the EGR1 pathway. Thus, it is likely that this gene  
10 activates sensory neuron cells, and to a lesser extent other neuronal cells, through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from JAK-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation.

15 This gene is expressed primarily in chondrosarcoma tissue, and to a lesser extent in glioblastoma and bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
20 not limited to, cancers of the bone and CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell  
25 types (e.g., skeletal, hematopoietic, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:109 as residues: Ala-15 to Gly-22, Asp-44 to Ile-53.

The tissue distribution in chondrosarcoma tissue, in conjunction with the detected biological activity in sensory neurons, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of  
35 neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning

disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Alternatively, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation) in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Furthermore, the tissue distribution in chondrosarcoma tissue indicates that the translation product of this gene is useful for the detection and/or treatment of cancers of cartilage, connective tissues, and synovium, for example, as well as cancers of other tissues where expression has been observed. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:13 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1011 of SEQ ID NO:13, b is an integer of 15 to 1025, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 4

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LKVPTCY SANT (SEQ ID NO:205). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in cerebellum and infant brain tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or developmental disorders, particularly neurodegenerative conditions in the central nervous system, and congenital defects. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., brain and other tissue of the nervous system, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, amniotic fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 110 as residues: Gly-40 to Lys-45.

The tissue distribution in brain and cerebellum tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating cell loss in the central nervous system due to trauma, ischaemia, or disease. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders.

Moreover, the expression within infant tissue suggests this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain



neurodegenerative disorders, such as spinal muscular atrophy (SMA). Therefore, the polynucleotides and polypeptides of the present invention are useful in treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:14 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 767 of SEQ ID NO:14, b is an integer of 15 to 781, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:14, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 5

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

WQVPAPVIPGXDPVRGARKRTLGVAGGWRRFERLWAGSLS (SEQ ID NO:206), SRSLALAAAPSSNGSPWRLGALCLQRPPVSKPLTPLQEE (SEQ ID NO:207). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in colon cancer cell line and glioblastoma tissue, and to a lesser extent in synovial fluid, placenta, and fetal liver tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers of the colon and glial cells. Similarly, polypeptides and

antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive tract, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., gastrointestinal tissue, synovial tissue, hepatic tissue, nervous tissue, vascular, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:111 as residues: Arg-12 to Asp-17, Leu-23 to Ala-34, His-37 to Gln-43, Thr-69 to Arg-86, Pro-140 to Lys-147, Lys-188 to Tyr-199.

The tissue distribution in cancerous colon tissues and glioblastoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosing and/or treating cancers of the colon and glia, as well as cancers of other tissues where expression has been observed. The protein product of this clone is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages.

The uses include bone marrow cell ex- vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The protein is useful for the modulation of the immune response to various tissues and cell types, thought particularly to developmental and gastrointestinal cell and tissues. The protein is useful for modulating apoptosis and may show utility in combating cancer and degenerative disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:15 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1026 of SEQ ID NO:15, b is an integer of 15 to 1040, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 6

When tested against K562 leukemia cell lines, supernatants removed from cells containing this gene activated the ISRE assay. Thus, it is likely that this gene activates leukemia cells, and to a lesser extent immune cells, in addition to other cells or cell-types, through the JAK-STAT signal transduction pathway. The interferon-sensitive response element is a promoter element found upstream of many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STAT pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in embryonic tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases affecting embryonal development and developmental abnormalities, in addition to cancer and degenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing fetus or embryo, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developing and differentiating tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:112 as residues: Arg-12 to Gly-18, Pro-51 to Lys-57, Glu-64 to Lys-78, Lys-102 to Lys-109.

5 The tissue distribution in embryonic tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis of developmental defects or as a growth or differentiation factor that may affect specific populations of cells. Furthermore, expression within embryonic tissue, in conjunction with the biological activity data, as well as other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may  
10 show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker  
15 and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:16 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the  
20 scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 698 of SEQ ID NO:16, b is an integer of 15 to 712, where both a and b correspond to the positions of nucleotide residues shown in  
25 SEQ ID NO:16, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 7

30 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:  
MEEEAYSKGFQEGCLKTKELQDLKEEEEEEQKSESPEEPEEV (SEQ ID NO:208),  
and/or EETEEEEKGPRSSKLEELVHFLQVMYPKLCQHWQVIW (SEQ ID NO:209).  
Polynucleotides encoding these polypeptides are also encompassed by the invention.

35 This gene is expressed primarily in brain tissue from patients with dementia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological diseases and disorders, including dementia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:113 as residues: Gln-53 to Thr-60.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful as a factor that may enhance survival of neuronal cells. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:17 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1309 of SEQ ID NO:17, b is an integer of 15 to 1323, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 8

5 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ILYLVWAFIPESWLNLSGLTYWPQKYWAVALPVYLLIAIVI (SEQ ID NO:210), YGFVLFLSSQFGFILYLVA (SEQ ID NO:211), TSPLDSIH TITD (SEQ ID NO:212), PLPERAIYGFVLFLSSQFGF (SEQ ID NO:213), and/or PTRGGSILCACPWGLPSRLGLSLRFSSPLRLPSRRLRENSALRLSKAPGK  
10 (SEQ ID NO:214). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in activated T cells, synovial cells, osteoblasts and microvascular endothelium, and to a lesser extent in fetal brain and hodgkins lymphoma tissues.

15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, proliferative disorders of the hematopoietic system, including lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are  
20 useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., T-cells and other cells and tissue of the immune system, bone, synovial tissue, endothelial cells, vascular cells and  
25 tissues, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:114 as residues: Glu-3 to Pro-10, Thr-91 to Glu-105.

The tissue distribution in immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders of the immune system involving abnormal growth of specific types of cells, as well as of other cell  
35 types where expression has been observed. Furthermore, elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene

product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Protein is useful in the detection, treatment, and/or prevention of skeletal and/or vascular disorders and conditions, which include, but are not limited to arthritis, stroke, embolism, microvascular disease, aneurysm, and atherosclerosis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:18 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 772 of SEQ ID NO:18, b is an integer of 15 to 786, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to a + 14.

## 20 FEATURES OF PROTEIN ENCODED BY GENE NO: 9

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: PPGCRNSARE (SEQ ID NO:215). Polynucleotides encoding these polypeptides are also encompassed by the invention.

25 This gene is expressed primarily in frontal cortex tissue of the brain, and in fetal liver/spleen tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, seizures and/or disorders associated with the central nervous system and hematopoietic systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., brain and other tissue of the nervous system, hepatic tissue, hematopoietic, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,

serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 5 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:115 as residues: Thr-56 to Arg-62.

The tissue distribution in frontal cortex tissue of the brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating seizure induced damage in the cortical regions of the central nervous system.

- 10 Furthermore, elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. The protein  
15 product of this clone is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex- vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

- 20 The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The protein is useful in modulating the  
25 immune response to neural cells and tissues, and particularly in regulating apoptosis, proliferative and/or degenerative conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

- Many polynucleotide sequences, such as EST sequences, are publicly available  
30 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:19 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
35 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 496 of SEQ ID NO:19, b is an integer of 15 to



510, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 10

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: PPGCRNSARE (SEQ ID NO:216). Polynucleotides encoding these polypeptides are also encompassed by the invention.

10 This gene is expressed primarily in frontal cortex tissue of the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders and diseases, particularly ischemic damage to the  
15 cortex. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., brain and other tissues of  
20 the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:116 as residues: Glu-29 to Gly-36.

The tissue distribution in frontal cortex tissue of the brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for reducing the damage resulting from ischaemic injury in the central nervous system. Furthermore,  
30 elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. Protein, as well as, antibodies  
35 directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:20 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 736 of SEQ ID NO:20, b is an integer of 15 to 750, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 11

When tested against K562 leukemia cell lines, supernatants removed from cells containing this gene activated the ISRE assay. Thus, it is likely that this gene activates leukemia cells, and to a lesser extent immune cells and tissues, in addition to other cells and cell-types, through the JAK-STAT signal transduction pathway. The interferon-sensitive response element is a promoter element found upstream of many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STAT pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in liver tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic and metabolic disorders and conditions, particularly hepatitis, cirrosis and hepatomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in liver tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or diagnosis for diseases of the liver, including cirrosis and hepatitis, and may act as a factor for the regeneration of cells of epithelial cell origin. Furthermore, additional disorders and/or diseases that the translation product of this gene is useful for in the detection and/or treatment of include hepatoblastoma, jaundice, hepatitis, and liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:21 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 824 of SEQ ID NO:21, b is an integer of 15 to 838, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 12

When tested against K562 cell lines, supernatants removed from cells containing this gene activated the ISRE (interferon-sensitive responsive element ) pathway. Thus, it is likely that this gene activates kidney cells, and to a lesser extent other uro-genital cells, through the JAK-STAT signal transduction pathway. ISRE is a promoter element found upstream in many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STAT pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GASSRPRLELGRLMGPKGVAVDRNXHIIVVDNKSCCVFTFQPNG (SEQ ID NO:217), KLVGRFGGRGATDRHFAGPHFVAVNNKNEIVVTDFHNHSVKVYS

(SEQ ID NO:218), ADGEFLFKFGSHGEGNGQFNAPTGVAVDSNGNIIVADWG  
NSR (SEQ ID NO:219), IXGIRXLWLLPVLYQHICRTTVWSTGPGTDLGWPCGG  
G (SEQ ID NO:220). Polynucleotides encoding these polypeptides are also  
encompassed by the invention.

5 This gene is expressed primarily in 7 week old embryonic tissue, and to a lesser  
extent in Jurkat T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are  
10 not limited to, developmental, urogenital, and immune disorders. Similarly,  
polypeptides and antibodies directed to these polypeptides are useful in providing  
immunological probes for differential identification of the tissue(s) or cell type(s). For a  
number of disorders of the above tissues or cells, particularly of the immune and  
urogenital systems, expression of this gene at significantly higher or lower levels may  
15 be routinely detected in certain tissues or cell types (e.g., immune, developmental,  
urogenital, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum,  
plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell  
sample taken from an individual having such a disorder, relative to the standard gene  
expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
20 individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID  
NO:118 as residues: Trp-29 to Gly-42, Gly-46 to His-51.

The tissue distribution in Jurkat cells indicates that polynucleotides and  
polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of  
25 a variety of immune system disorders. Expression of this gene product in T-cells  
indicates the protein may play a role in regulating the proliferation; survival;  
differentiation; and/or activation of potentially all hematopoietic cell lineages, including  
blood stem cells. Elevated levels of expression of this gene product in T cell lineages  
indicates that it may play an active role in normal T cell function and in the regulation of  
30 the immune response. For example, this gene product may be involved in T cell  
activation, in the activation or control of differentiation of other hematopoietic cell  
lineages, in antigen recognition, or in T cell proliferation.

This gene product may be involved in the regulation of cytokine production,  
antigen presentation, or other processes that may also suggest a usefulness in the  
35 treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed  
in cells of lymphoid origin, the natural gene product may be involved in immune  
functions. Therefore it may be also used as an agent for immunological disorders

including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis.

In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus.

Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:22 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1047 of SEQ ID NO:22, b is an integer of 15 to 1061, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 13

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: MEWEGGAIRHPSTELG (SEQ ID NO:221), RPTRPPDGCH

PSSCCRMEAAMEWEGGAIRHPSTELGI (SEQ ID NO:222). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in endometrial stromal cells, and to a lesser extent in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive disorders and diseases, particularly diseases of the female reproductive system including endometriosis, and diseases of the immune system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive tissues, immune system tissues, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:119 as residues: Pro-30 to Ala-35.

The tissue distribution in endometrium indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or diagnosis of endometriosis. Furthermore, this gene could be transfected in gene-replacement treatments into the cells of the endometrium, and the protein products could be produced. These treatments could be performed during artificial insemination for the purpose of increasing the likelihood of implantation and development of a healthy embryo. In this case the gene or its gene product could be administered at later stages of pregnancy to promote healthy development of the endometrium. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:23 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 870 of SEQ ID NO:23, b is an integer of 15 to 884, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to a + 14.

## 10 FEATURES OF PROTEIN ENCODED BY GENE NO: 14

When tested against Jurkat T-cell cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates T-cells, and to a lesser extent other immune cells, through the JAK-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in stomach cancer tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal disorders and cancers, particularly of endothelial tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the metabolic and gastrointestinal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., endothelial, gastrointestinal, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:120 as residues: Met-1 to Ser-11.

The tissue distribution in stomach cancer tissue, combined with the observed GAS biological activity, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of stomach cancer and other proliferative disorders, as well as cancers of other tissues where expression has been observed. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:24 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 697 of SEQ ID NO:24, b is an integer of 15 to 711, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to a + 14.

## **FEATURES OF PROTEIN ENCODED BY GENE NO: 15**

The translation product of this gene was shown to have homology to the human reverse transcriptase, which may suggest that the translation product of this gene is useful as part of a viral vaccination strategy, particularly for retroviruses which require the participation of their encoded reverse transcriptase for provirus rescue and propagation (See Genbank Accession No.gil439877). One embodiment of this gene comprises polypeptides of the following amino acid sequence: ECQEYEILEHCWWECKLVQPFWKSSCRIPAARGIH (SEQ ID NO:223), HCWWE CKLVQPFWK (SEQ ID NO:224), and/or FTFPPT (SEQ ID NO:225). An additional embodiment is the polynucleotides encoding these polypeptides. The gene encoding the disclosed cDNA is believed to reside on chromosome 10. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 10.

This gene is expressed primarily in human chronic synovitis tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are



not limited to, joint and skeletal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovium, expression of this gene at

5 significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., musculoskeletal, immune, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily

10 fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:121 as residues: Glu-28 to Ser-33.

The tissue distribution in chronic synovitis tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or

15 treatment of joint and musculoskeletal conditions. In addition, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation) in the diagnosis or treatment of various autoimmune

20 disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or

25 immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:25 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

30 scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 493 of SEQ ID NO:25, b is an integer of 15 to 507, where both a and b correspond to the positions of nucleotide residues shown in

35 SEQ ID NO:25, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 16

The translation product of this gene shares sequence homology with mouse  
 5 testin, which is thought to be important in normal cell function, particularly in testes  
 (See Genebank Accession No.gil475210). In specific embodiments, polypeptides of the  
 invention comprise the following amino acid sequence:

HHHLRVGSPWSPETGTAVHGAHPQGEAASDRHRGCFYRRRQLMHQLPIYDQ  
 DPSRCRGLLENELKLMEEFVKQYKSEALGVGEVALPGXGWLAKKEEGKQQEK  
 10 PEGAETXAXTTNGXXSDPSKEEAC (SEQ ID NO:226), TYEWAPP (SEQ ID  
 NO:227), PKEKQPV (SEQ ID NO:228), and/or PRPANLAIQPPLSPLRALAPLPEK  
 PGAVPPPQKR (SEQ ID NO:229). Polynucleotides encoding these polypeptides are  
 also encompassed by the invention.

This gene is expressed primarily in placental tissue and osteoblasts, and to a  
 15 lesser extent, in prostate, smooth muscle tissue, heart tissue, fibroblasts, and adipose  
 tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 20 not limited to, vascular, cardiovascular, reproductive, skeletal, metabolic, and growth  
 disorders. Similarly, polypeptides and antibodies directed to these polypeptides are  
 useful in providing immunological probes for differential identification of the tissue(s)  
 or cell type(s). For a number of disorders of the above tissues or cells, particularly of  
 the vascular and cardiovascular, reproductive and skeletal systems, expression of this  
 25 gene at significantly higher or lower levels may be routinely detected in certain tissues  
 or cell types (e.g., vascular, cardiovascular, developmental, reproductive, skeletal, or  
 cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum,  
 plasma, seminal fluid, urine, synovial fluid and spinal fluid) or another tissue or cell  
 sample taken from an individual having such a disorder, relative to the standard gene  
 30 expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
 individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID  
 NO:122 as residues: Pro-40 to Lys-48, Cys-50 to Leu-59, Asp-62 to Ile-69, Pro-138 to  
 Pro-143.

35 The tissue distribution in placental tissue, osteoblasts, prostate tissue, and  
 adipose tissue, combined with the homology to the murine testin protein, indicates that  
 polynucleotides and polypeptides corresponding to this gene are useful for the study,

diagnosis and/or treatment of disorders affecting normal cell functioning, including reproductive, developmental and metabolic disorders. The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function.

Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis or may play a role as a therapeutic in ameliorating or preventing stroke, aneurysm, atherosclerosis, and emboli. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

The tissue distribution in smooth muscle and heart tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of conditions and pathologies of the cardiovascular system, such as heart disease, restenosis, atherosclerosis, stroke, angina, thrombosis, and wound healing. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other

hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues

- 5 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:26 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.
- 10 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2218 of SEQ ID NO:26, b is an integer of 15 to 2232, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 17

- 20 The translation product of this gene was shown to have homology to the LW opsin-long-wave visual pigment gene, which is known to play an integral role in establishing long wave spectrum absorption in higher primates (See Genebank Accession No.bbsl162162 ). The gene encoding the disclosed cDNA is believed to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

- 25 This gene is expressed primarily in melanocytes, human cornea, and to a lesser extent, in spleen and pineal gland tissues.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders involving the epithelial, hemopoietic, visual, and endocrine systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the epithelial, endocrine and hemopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., epithelial, endocrine, hemopoietic, visual, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, aqueous humor, vitreous humor,
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synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5           The tissue distribution in human cornea, combined with its homology to a conserved opsin gene, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, diagnosis, and/or prevention of a variety of visual disorders and afflictions, and may potential play a role in ameliorating, treating, or preventing biological clock disorders, DNA repair aberrations, and cancer.

10       Alternatively, the tissue distribution in melanocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma,

15       malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and

20       xanthelasma. Moreover, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athletes foot, and ringworm). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors

25       Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:27 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

30       Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 626 of SEQ ID NO:27, b is an integer of 15 to 640, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 18

The translation product of this gene shares sequence homology with adaptor protein 150, which is thought to be important in post-synthesis protein sorting to vacuoles.

This gene is expressed primarily in testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, endocrine, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:124 as residues: Arg-24 to Arg-41, Pro-56 to Trp-64.

The tissue distribution in testes tissue, and the homology to adaptor protein 150, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, prevention, and/or treatment of various metabolic disorders such as Tay-Sachs disease, phenylketonuria, galactosemia, porphyrias, and Hurler's syndrome. Alternatively, expression in human testes would suggest a role for this gene in the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes.

Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to

identify binding agents, as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to be useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:28 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 399 of SEQ ID NO:28, b is an integer of 15 to 413, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 19

The translation product of this gene shares sequence homology with the human acetyl coenzyme A:cholesterol acyltransferase II protein, which is thought to be important in metabolism of oxidized LDL (See Genebank Accession No.W43406). As such, the translation product of this gene may be useful in the diagnosis, treatment, and/or prevention of lipid disorders, and their accompanying secondary conditions such as atherosclerosis or hyperlipidaemia. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

AHAVWRPGVLPGLVELRVCHLLLAELEHPCAQVVHQVGGVCVCVMWNMA  
VNLNRFPCPLLCRHFYKPMRLRGSSKWMARTGVFLASAFFHEYLVSVPLRMF  
RLWAFTGMMQAQIPLAWFVGRFFQGNYGNAAVWLSLIIGQPIAVLMYVHDYY  
VLN YEAPAAEA (SEQ ID NO:230), YFLFAPTL (SEQ ID NO:231), NLNRFPCPL  
LCRHFYK (SEQ ID NO:232), QGNYGNAAVWLSLIIG (SEQ ID NO:233), LYY  
FLFAPTL CYELNFP (SEQ ID NO:234), EMLFFTQLQVGLIQQWMVPTIQNSMK  
(SEQ ID NO:235), VTYFWQNWNIPVHKWCIR (SEQ ID NO:236), PFKDMDYS

RIIERLLKLAVPN HLIWLIFYWLFHSCNVAELMQFGDREFYRDWWNSE  
 (SEQ ID NO:237), RHFYKPMLRRGSSKWMARTGVFLASAFFHEYLVSVPLRM  
 FRLWAFTGM (SEQ ID NO:238), and/or MAQIPLAWFVGRFFQGNYGNAAVWLS  
 LIIGQPIAVLMYVHDYYVLNY (SEQ ID NO:239). Polynucleotides encoding these  
 5 polypeptides are also encompassed by the invention.

This gene is expressed primarily in pancreatic tumors and breast cancer, and to a lesser extent, in early stage human brain and fetal liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
 10 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and central nervous system disorders, including cancers thereof. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the  
 15 developmental, metabolic, and the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., endocrine, neural, metabolic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a  
 20 disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:125 as residues: Gly-43 to Ser-56.

The tissue distribution in cancerous and neural tissues, combined with the  
 25 homology to acetyl coenzyme A, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis and/or treatment of disorders of the central nervous system, and metabolic and developmental disorders, including Tay-Sachs disease, phenylketonuria, galactosemia, porphyrias, and Hurler's syndrome. Alternatively, the tissue distribution in various cancers indicates that  
 30 polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of cancer and other proliferative disorders, as well as cancers of other tissues where expression has been observed. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Similarly, embryonic development  
 35 also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed



against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:29 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1108 of SEQ ID NO:29, b is an integer of 15 to 1122, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 20

The translation product of this gene has been found to have homology to the vacuolar protein sorting homolog r-vps33b of *Rattus norvegicus*, which has been implicated in Golgi-to-lysosome trafficking (See Genebank Accession No.gil1477470). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SGXWQGLDEVVRLNLNXSDFAFTD (SEQ ID NO:240) and/or GSLAKRSNFRAISKKLNLIPRVDGEYDLKVPRDMAYVFXGAYVPLSCRIIE QVLERRXAGP (SEQ ID NO:241). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in thymus and amygdala tissues, and to a lesser extent in infant brain tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic, immune, or central nervous system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the metabolic and central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, neural, or

cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:126 as residues: Met-1 to Glu-10, Gly-35 to Tyr-40.

The tissue distribution in fetal brain and amygdala tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Alternatively, expression in thymus tissue, combined with the homology to a vacuolar protein, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Expression of this gene product in thymus indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein is useful in the treatment, detection, and/or prevention of neural disorders involving aberrant neurotransmitter secretion. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:30 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 764 of SEQ ID NO:30, b is an integer of 15 to 778, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:30, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 21

The translation product of this gene was shown to have homology to the CIT987SK-A-589H1\_1 protein (See Genebank Accession No. gil2342743). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: EVINTLADHRHRGTDGFGSPWLLIITVFLRSYKFAISLCTSYLCV SFLKTI FPSQNGHDGSTDVQQRARRSNXRRQEGIKIVLEDIFTLWRQVETKVRA KIRKMKVTTKVNRHDKINGKRKTAKEHLRKL SMKEREHGEKERQVSEAAE NGKLD MKEIHTYMEMFQRAQVCGGGQRTTTDAKSPL LQESLFATG (SEQ ID NO:242), ICVKTFPPLALQVRMAAXEHRHSSGLPXWPYLTAE TLKNRMGHQ PPPPTQQHSIXDNSLSLKTPAECLLYPLPPSADDNLKTPXECLLTPLPPSAPPSA DDNLKTPPECVC SLPFHPQLHPQRMISRHLPSVSAHSPSTLSG (SEQ ID NO:243), RARRSNXRRQEGIKIVLEDI (SEQ ID NO:244), and/or LSLKTPAECLLY PLPP (SEQ ID NO:245). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in cerebellum and other brain tissues such as amygdala and frontal cortex, testes tumor, and to a lesser extent, in synovium and adipocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, neural, or skeletal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system and reproductive

system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, skeletal, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:127 as residues: Ala-23 to Cys-34.

The tissue distribution in brain tissues such as cerebellum, frontal cortex, and amygdala indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and/or treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception.

Elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation) in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:31 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more

- 5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2462 of SEQ ID NO:31, b is an integer of 15 to 2476, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 22

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: FLLIESYQKLNRKTNLSLHVFLFHTEV (SEQ ID NO:246).

- 15 Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human testicular tumors.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or endocrine disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, endocrine, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.
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- The tissue distribution in testicular cancer tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents, as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to be useful in the treatment and/or diagnosis
- 35

of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Alternatively, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders, as well as cancers of other tissues where expression has been observed. Expression within tumor tissues and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:32 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 677 of SEQ ID NO:32, b is an integer of 15 to 691, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 23

This gene is expressed primarily in resting T cells and CD34(+) cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily

fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5           The tissue distribution in CD34(+) cells and T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example,  
10 this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

          Expression of this gene product in T-cells further indicates the protein may play  
15 a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin,  
20 the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of  
25 various blood lineages, and in the differentiation and/or proliferation of various cell types.

          The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very  
30 wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating  
35 anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities

(e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others.

- 5 Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
10 ID NO:33 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
15 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 686 of SEQ ID NO:33, b is an integer of 15 to 700, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.

## 20 **FEATURES OF PROTEIN ENCODED BY GENE NO: 24**

The translation product of this gene was shown to have homology to the yeast WD-40 domain-containing YCW2 protein (See Genebank Accession No.R85881), which is thought to modulate protein-protein interactions via its WD-40 domain  
25 between proteins involved in intracellular signalling. An example of such an interaction is between protein kinase C and receptors of activated protein kinase. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

YALRTGAFEPAEASVNPQDLQGSLQELKERALSRYNLVRGQGPRLVSGSDDF  
30 TLFLWSPAEXKKPLTRMTGHQALINQVLFSPDSRIVASASFDKSIKLWDGRT  
GKYLASLRGHVAAVYQIAWSADSRLLVSGSSXQHTEGVGCEGP EAGHGPARG  
PRG (SEQ ID NO:247), and/or LKERALSRYNLVRGQGPRLV (SEQ ID NO:248).  
Polynucleotides encoding these polypeptides are also encompassed by the invention.

35 This gene is expressed primarily in infant brain and breast tissues, and to a lesser extent, in various other endocrine and neuronal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a



biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental, and neurodegenerative diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and central nervous systems; expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, neural, reproductive, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, breast milk, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:130 as residues: Pro-13 to Ser-20.

The tissue distribution in infant brain and neural tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and/or treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:34 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1708 of SEQ ID NO:34, b is an integer of 15 to 1722, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.

5

## FEATURES OF PROTEIN ENCODED BY GENE NO: 25

The translation product of this gene shares sequence homology with preprotein translocase, which is thought to be important in mitochondrial protein import (See Genbank Accession No.P39515). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

MPTPSMRANRMPPIAEPTMASGPLRAASTAPVNAPLVIEFQGSSLP RSRTRPQS  
 MVENRPPHTAKLPPIWGARILTALALPLNRCRIPTGALRKPLMAWKTPPPMTPI  
 15 VKAPPQSSTIRHGQGS RAYSGRVGGRVG (SEQ ID NO:249), GARILTALALPL  
 NRCRIPTGALRK (SEQ ID NO:250), PTRPPTRPEYAREPCPWRIVDDCGGAF  
 TMGVIGGGVFQ (SEQ ID NO:251), AIKGFRNAPVGIRHRLRGSANAVRIRAPQI  
 GGSFAVWGG (SEQ ID NO:252), LFSTIDCGLVRLRGKEDPWN SITSALTGAV  
 LAARSGPLA (SEQ ID NO:253). Polynucleotides encoding these polypeptides are also  
 20 encompassed by the invention.

This gene is expressed primarily in activated T-cells, and to a lesser extent, in other tissues and transformed cell lines.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
 25 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory, metabolic, and immune conditions or diseases, particularly immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of  
 30 the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the  
 35 standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:131 as residues: Tyr-25 to Ala-33, Asp-39 to Thr-49, Ala-51 to His-61.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Furthermore, elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, homology to a known mitochondrial protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, prevention, and/or treatment of various metabolic disorders such as Tay-Sachs disease, phenylketonuria, galactosemia, porphyrias, and Hurler's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:35 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 864 of SEQ ID NO:35, b is an integer of 15 to 878, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 26

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: IRHERKSARACCPLTGAQRRGQALPTPRAGPGHSPAPV  
 10 (SEQ ID NO:254), APSAPQEDGGSPAPQGQPDGPGAGQPAQLGPLLAFL (SEQ ID NO:255), PLLHQDCKESPHLGSSGSPVQALDLSSIQTRTAVSCVDGVRLWA (SEQ ID NO:256). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 6. Accordingly, polynucleotides related to this invention are useful as a  
 15 marker in linkage analysis for chromosome 6.

This gene is expressed primarily in bone marrow and brain tissues, and to a lesser extent in placental tissue and other sources.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
 20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, neurological, and reproductive disorders or diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and  
 25 nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, neural, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression  
 30 level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:132 as residues: Ser-42 to Arg-47, Thr-115 to Ser-127, Ser-130 to Trp-136.

The tissue distribution in bone marrow indicates that polynucleotides and  
 35 polypeptides corresponding to this gene are useful for the treatment and/or diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of

cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Alternatively, the tissue distribution in brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:36 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more

- 5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 940 of SEQ ID NO:36, b is an integer of 15 to 954, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 27**

This gene is expressed primarily in activated T-cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as
- 15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic and immune disorders or diseases, particularly inflammatory conditions and immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
- 20 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or
- 25 another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of
- 30 immune system disorders. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Furthermore, expression of
- 35 this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Expression of this gene product in T-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation;

and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed

5 in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of

10 stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very

15 wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating

20 anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for

25 treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

30 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:37 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

35 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 779 of SEQ ID NO:37, b is an integer of 15 to

793, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 28

This gene is expressed primarily in placental tissue, and to a lesser extent, in various infant and adult tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, placental, reproductive, and metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system and placenta, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developing, reproductive, placental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, amniotic fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in placental tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis, treatment, and/or prevention of various growth and reproductive disorders. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.



Alternatively, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification.

Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:38 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 545 of SEQ ID NO:38, b is an integer of 15 to 559, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 29

The translation product of this gene shares sequence homology with the C2H2 type zinc finger protein, which is important in gene regulation. Furthermore, since the C2H2 zinc finger protein has significant homology to the human BRCA1-associated protein (hBRAP), this gene may be implicated as playing a central role in the modulation of cell cycle control. (See Genebank Accession Nos. gil328223 and W52187, respectively). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: HRLQVFSFPILGSHN (SEQ ID NO:257). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in several transformed cell lines, and to a lesser extent, in some normal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and growth disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:135 as residues: Gly-25 to Asn-31, Leu-42 to Lys-50.

The tissue distribution in transformed cell lines, combined with the homology to both a zinc-finger protein as well as a transforming protein associated with human breast cancer, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of cancer and other proliferative disorders. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Protein is useful in modulating apoptosis which would be useful in the detection, treatment, and/or prevention of degenerative and/or proliferative conditions. Protein, as well as,

antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:39 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1249 of SEQ ID NO:39, b is an integer of 15 to 1263, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 30

This gene is expressed primarily in adult bladder tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal and urogenital diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the excretory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., urogenital, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult bladder tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis, treatment, and/or prevention of various gastrointestinal and urogenital disorders and afflictions. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the

specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:40 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 441 of SEQ ID NO:40, b is an integer of 15 to 455, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 31

The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

This gene is expressed primarily in infant brain and placental tissues, and to a lesser extent, in various normal and neoplastic cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and reproductive disorders. Similarly, polypeptides and

antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:137 as residues: Gly-35 to Ser-41, Glu-45 to Tyr-57.

The tissue distribution in infant brain tissue and placental tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and/or treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception.

In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, the expression within infant tissue and other cellular sources marked by proliferating cells suggests this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain neurodegenerative disorders, such as spinal muscular atrophy (SMA). Therefore, the polynucleotides and polypeptides of the present invention are useful in treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:41 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1114 of SEQ ID NO:41, b is an integer of 15 to 1128, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 32

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GKVEIEVFIFPYEYPVVPTPLIKNTILYPLSLFCTFIKNQFSIYLWIKFFIF (SEQ ID NO:258). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in B-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and haemopoietic disorders, including cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, haemopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:138 as residues: Trp-27 to Ile-39.

The tissue distribution in B-cell lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in B-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:42 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 634 of SEQ ID NO:42, b is an integer of 15 to 648, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 33**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: RATTHVSREFFGHT (SEQ ID NO:259). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in B-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic system disorders, including cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in B-cell lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in B-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility);



chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:43 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 722 of SEQ ID NO:43, b is an integer of 15 to 736, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 34

This gene is expressed primarily in prostate tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases or disorders of the prostate and reproductive organs. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, prostatic, and cancerous and wounded tissues) or bodily fluids (e.g., seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:140 as residues: Arg-18 to Ser-29.

The tissue distribution in prostate tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or diagnosis of disorders of the reproductive system and prostate. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein is useful as a contraceptive, either directly or indirectly. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:44 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 586 of SEQ ID NO:44, b is an integer of 15 to 600, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 35

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

- 5 TLFSMFSGPLGRQTQLDFRADIGEENMALSVLSPDKCYLYT (SEQ ID NO:260)  
and/or HPNLKRKCISLGFKHCNRYKAKIKTCCKVQKKKKKKKKKKKKKKGR  
(SEQ ID NO:261). Polynucleotides encoding these polypeptides are also encompassed by the invention.

10 This gene is expressed primarily in endometrium, osteoclastoma, and bladder tissues, and to a lesser extent in T-cells, infant brain and other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders or diseases of the skeletal, developmental, reproductive, and  
15 urogenital system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the urogenital, skeletal and haemopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues  
20 or cell types (e.g., endothelial, skeletal, reproductive, urogenital, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
25 having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:141 as residues: Gly-8 to His-18.

The tissue distribution in endometrium, T-cells, osteoclasts, and bladder tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for  
30 the treatment and/or diagnosis of disorders of the urogenital, skeletal, and haemopoietic systems. Elevated levels of expression of this gene product in osteoclastoma indicates that it may play a role in the survival, proliferation, and/or growth of osteoclasts. Therefore, it may be useful in influencing bone mass in such conditions as osteoporosis. Alternatively, this gene could be transfected in gene-replacement  
35 treatments into the cells of the endometrium, and the protein products could be produced. These treatments could be performed during artificial insemination for the purpose of increasing the likelihood of implantation and development of a healthy

embryo. In this case, the gene or its gene product could be administered at later stages of pregnancy to promote healthy development of the endometrium.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:45 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 673 of SEQ ID NO:45, b is an integer of 15 to 687, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 36

This gene is expressed primarily in induced T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders or diseases of the immune or haemopoietic system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, haemopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:142 as residues: Arg-6 to Lys-13, Tyr-19 to Val-27, Ser-40 to Tyr-46.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Elevated levels of expression of this gene product indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

Further, expression of this gene product in T-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:46 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 683 of SEQ ID NO:46, b is an integer of 15 to 697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 37

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: HSGVQTIAFGLEC (SEQ ID NO:262). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in induced T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders or diseases of the immune and haemopoietic systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in

T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

5 Further, expression of this gene product in T-cells indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by  
10 boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may  
15 have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available  
20 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:47 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 272 of SEQ ID NO:47, b is an integer of 15 to 286, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.

30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 38**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KVQDRDGKERRKQEEVKLGRWCQWH (SEQ ID NO:263).  
35 Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 3.

Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in induced T-cells, and to a lesser extent in neutrophils and bone marrow.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases or disorders of the haemopoietic and immune system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing  
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., haemopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine,  
15 synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID  
20 NO:144 as residues: Ser-17 to Trp-22, Lys-34 to Arg-39.

The tissue distribution in immune cells and tissues, such as T-cells, bone marrow, and neutrophils, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Expression of this gene product in T cells and neutrophils  
25 strongly indicates a role for this protein in immune function and immune surveillance. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen  
30 recognition, or in T cell proliferation.

The polypeptides or polynucleotides are also useful to enhance or protect proliferation, differentiation, and functional activation of hematopoietic progenitor cells (e.g., bone marrow cells), useful in treating cancer patients undergoing chemotherapy or patients undergoing bone marrow transplantation. Furthermore, expression of this  
35 gene product in tonsils indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the



regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:48 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 844 of SEQ ID NO:48, b is an integer of 15 to 858, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 39

5 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ACGAPEEAGG (SEQ ID NO:264). Polynucleotides encoding these polypeptides are also encompassed by the invention. The translation product of this gene shares sequence homology with a *C. elegans* protein F21D5.6 (See Genbank Accession No. gil3876107) which is thought to be important in development.

10 This gene is expressed primarily in T-cells and haemopoietic tissues, and to a lesser extent in several other tissues and organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic, immune, and/or developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, developmental, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:145 as residues: Leu-24 to Asn-33, Ala-104 to Lys-109, Thr-142 to Thr-163, Leu-167 to Asn-172, Asp-198 to Asp-207, Glu-223 to Lys-230, Leu-232 to Ser-238, Pro-242 to Ser-252, Glu-254 to Lys-278.

30 The tissue distribution in T-cells and immune cells and tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation. Expression of this gene product in T cells also strongly indicates a role for

this protein in immune function and immune surveillance. Furthermore, expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. Therefore, the protein may show utility in the treatment of various hematopoietic disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages.

The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein is useful in the treatment, detection, and/or prevention of developmental disorders and conditions, particularly congenital defects and metabolic conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:49 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1293 of SEQ ID NO:49, b is an integer of 15

to 1307, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 40

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LFSSFLGDTTVHKVLSRATLHLHPAPYLTGVDSYS (SEQ ID NO:265) and/or DFSSYSHPSLGTQLSIRCYPEPHCICTQHHTSQESTPTL (SEQ ID NO:266). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in stimulated T-cells, and to a lesser extent in smooth muscle tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, vascular and cardiovascular disorders or diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the haemopoietic and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., vascular, haemopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:146 as residues: Met-1 to Thr-10.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of immune system disorders. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Elevated levels of expression of this gene product in T cell lineages indicates that it may play an active role in normal T cell function and in the regulation of the immune response. For

example, this gene product may be involved in T cell activation, in the activation or control of differentiation of other hematopoietic cell lineages, in antigen recognition, or in T cell proliferation.

Furthermore, expression of this gene product in T-cells indicates the protein  
 5 may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. Therefore, this indicates that the protein is useful for treating various hematopoietic disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include  
 10 bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors  
 15 of various blood lineages, and in the differentiation and/or proliferation of various cell types.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed  
 20 in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of  
 25 stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the tissue distribution in smooth muscle tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of conditions and pathologies of the cardiovascular system, such as heart disease, restenosis,  
 30 atherosclerosis, stroke, angina, thrombosis, and wound healing. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
 35 ID NO:50 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 592 of SEQ ID NO:50, b is an integer of 15 to 606, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 41

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: APQKFPXGFFFFFLFSRRKKQCSKVQNTGAGAIQTQV (SEQ ID NO:267), QLLTSPTFSTVLSNYTCQAPSQWTDWQALLPTGIQTEH (SEQ ID NO:268), HQGWDKQKQCKRKCEHEHAPLHHNLWKQSGKTRLGD (SEQ ID NO:269). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in CD34 depleted blood cells, and to a lesser extent in prostate cancer tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, or reproductive diseases and disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the haemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, seminal fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:147 as residues: Glu-9 to Thr-17, Thr-19 to His-34, Thr-36 to Thr-42, Gln-44 to Lys-53.

The tissue distribution in CD34 depleted blood cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or diagnosis of hematopoietic related disorders such as anemia, pancytopenia,

leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. Expression of this gene product in CD34 depleted blood cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including

5 blood stem cells.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against

10 the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion

15 of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection,

20 inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents

25 that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities although no evidence for any is provided in the specification. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer,

30 autoimmune diseases and allergy); regulation of haematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation of growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumours); haemostatic or thrombolytic activity (e.g., for

35 treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative disease; for regulation of metabolism, behaviour, and many others.

Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. The protein is useful as a contraceptive, in addition to its applicability as a diagnostic for prostate cancer or other reproductive disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:51 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 533 of SEQ ID NO:51, b is an integer of 15 to 547, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 42**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KHVIFFMFISNLFILCFLFRPTKTTV (SEQ ID NO:270). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in immune system cells, such as T-cells, tonsils, and primary dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tonsillitis and other infectious conditions; immune dysfunction, particularly immunodeficiencies; hematopoietic disorders; lymphomas and leukemias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the



expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:148 as residues: Lys-74 to Tyr-79.

5           The tissue distribution in immune system cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of infectious diseases such as tonsillitis, in a non-surgical way or without the use of antibiotics. It could be used to trigger the body's own defense mechanisms to fight infections. Likewise, expression of this gene product in a variety of immune or blood  
10 cells indicates a general role in hematopoietic function, and it may control the proliferation, survival, or differentiation of a variety of blood cell lineages. Expression of this gene product in tonsils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of  
15 cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for  
20 immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

25           Alternatively, it may be involved in immune functions, such as immune surveillance or immune modulation, or may be involved in the recruitment of blood cells to sites of injury or inflammation. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional  
30 supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy);  
35 stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumors);

hemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding

5 nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

10 ID NO:52 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

15 a-b, where a is any integer between 1 to 851 of SEQ ID NO:52, b is an integer of 15 to 865, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.

## 20 **FEATURES OF PROTEIN ENCODED BY GENE NO: 43**

The translation product of this gene shares sequence homology with the P195 protein of Plasmodium falciparum which is thought to be important in the incidence of malarial infection.

25 This gene is expressed primarily in activated helper T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Malaria and other insect borne blood diseases; defects in immune

30 modulation; immune dysfunction; susceptibility to general infections. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected

35 in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a

disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to the P195 protein of plasmodium falciparum indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment or diagnosis of malaria and other blood diseases where the peptide of the P195 protein could be used as a vaccine for malaria immunity. Likewise, expression of this protein by helper T cells indicates that it may play a more general role in immune system function, and may be involved in immune surveillance, immune modulation, or in host defenses.

Alternatively, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:53 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 675 of SEQ ID NO:53, b is an integer of 15 to 689, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 44

The translation product of this gene was shown to have homology to the conserved opioid binding protein/cell adhesion molecule, which is thought to be important in the dual role of binding intracellular opioids, in addition to the facilitation of cell-cell contact (See Genbank Accession No. P11834). When tested against PC12 (Sensory neuron) cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) pathway. Thus, it is likely that this gene activates sensory neuron cells, or more generally, neuronal cells, in addition to other cells or cell-types, through the EGR1 signal transduction pathway.

EGR1 is a separate signal transduction pathway from JAK-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KWKGDLHCILGLLA (SEQ ID NO:272). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in hypothalamus, and other brain tissues such as infant and adult whole brain, frontal lobe tissue, and amygdala tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, anorexia/bulimia, high blood pressure, migraine headaches, insomnia, or other neural disorders associated with anomalous neural chemistry or neurotransmitter activation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, endocrine, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the hypothalamus and other neural tissues, in conjunction with the biological activity data and the homology to an opioid binding protein, indicates that polynucleotides and polypeptides corresponding to this gene are

useful for the detection and/or treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, perception, in addition to disorders associated with neurotransmitter homeostasis or regulation. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, expression within the hypothalamus may suggest that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein is useful in the amelioration and prevention of pain. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:54 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 501 of SEQ ID NO:54, b is an integer of 15 to 515, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 45**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LAPSSVGSAS (SEQ ID NO:273), REATKNPHTHRSTPHAAGSQLNVPPQPCFPLHHQIKTSP (SEQ ID NO:274), SQ TIFKQSRHRCD SRQESTWLCSHEKDATKMMHLNDNS (SEQ ID NO:275), and/or VTGSPILQLALLQLPAWPLRGRLRGKRHCTGLNLAISGNGGEWGGRGE (SEQ

35

ID NO:276). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hypothalamus tissue which was derived from patients with schizophrenia.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, schizophrenia and other neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing  
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, endocrine, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal  
15 fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hypothalamus tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and/or treatment of  
20 neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception.

25 In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, the expression within the hypothalamus may suggest that the polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or  
30 prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies directed against the protein  
35 may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:55 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 733 of SEQ ID NO:55, b is an integer of 15 to 747, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 46

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: IRHEDEVKLEWS (SEQ ID NO:277). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hypothalamus, derived from patients with schizophrenia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disorders, particularly schizophrenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, endocrine, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hypothalamus indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania,

dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, expression within the hypothalamus indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:56 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 662 of SEQ ID NO:56, b is an integer of 15 to 676, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 47

Contact of cells with supernatant expressing the product of this gene has been shown to increase the permeability of the plasma membrane of THP-1 cells to calcium. Thus it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product binds a receptor on the surface of the plasma membrane of monocytes, or more generally, immune or hemopoietic cells, in addition to other cell-lines or tissue cell types. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating monocytes. The translation product of this gene shares sequence homology with NADH dehydrogenase ubiquinone which is known to be important for the establishment of an electron transport chain in



mitochondrial metabolism(See Genebank Accession No.gil1935056). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SLHSSAVAATYKYVNMQDPEMDMKSVTDRAARTLL (SEQ ID NO:278), WTELFRLGLGMTLSYLFREPATINYPFEKGPLSPRFRGEHALRRYPS  
 5 GEERCIACKLCEAI (SEQ ID NO:279), CPAQAIEAEPRADGSRRTTRYDIDMTKC IYCGFCQEACPVDAIVEGPNFEFSTETH (SEQ ID NO:280), and/or GDKWEAEIA ANIQADYLYR (SEQ ID NO:281). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in pituitary, and to a lesser extent, in kidney  
 10 and liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and/or metabolic disorder and diseases, particularly  
 15 mitochondrial disorders; kidney dysfunction; abnormal growth; liver disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine, hepatic, renal, and haemolymphoid systems, expression of this gene at significantly higher or  
 20 lower levels may be routinely detected in certain tissues or cell types (e.g.,endocrine, metabolic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.,lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily  
 25 fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:153 as residues: Gly-20 to Leu-27, Pro-85 to Leu-91, Arg-102 to Glu-108.

The tissue distribution in liver, combined with the homology to the conserved NADH dehydrogenase ubiquinone and the detected calcium flux activity suggest that  
 30 polynucleotides and polypeptides corresponding to this gene are useful for the detection or treatment of the problems associated with energy metabolism, since it is the first component of the electron transport chain. This may result specifically in renal dysfunction, abnormal growth, and/or liver disorders such as Tay-Sachs disease, phenylketonuria, galactosemia, porphyrias, and Hurler's syndrome. Alternatively,  
 35 expression within the pituitary indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's

Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:57 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 818 of SEQ ID NO:57, b is an integer of 15 to 832, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The translation product of this gene shares sequence homology with an insulin-like growth factor-binding complex and acid-labile subunit (ALS) which is thought to be important in protein-protein interactions involved in intracellular signalling. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

SAADPATQPGDSRALPEPRGVPAVHPAGSGSEWERPPPAAPSPEHRDK (SEQ ID NO:282), and/or DSRALPEPRGVPAVHPAGSGSEWE (SEQ ID NO:283).

Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in merkel cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders, particularly diabetes. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lymphoid or endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., endocrine, proliferating, and cancerous and

wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:154 as residues: Ala-68 to His-74.

The tissue distribution in merkel cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly diabetes, Addison's  
10 disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes.

Alternatively, the homology to an insulin-like growth factor indicates that  
15 polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders, and may potentially play a role in the regulation of cellular division. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could  
20 again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
25 ID NO:58 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
30 a-b, where a is any integer between 1 to 989 of SEQ ID NO:58, b is an integer of 15 to 1003, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 49

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: EFGTSWV (SEQ ID NO:284). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in kidney cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal, urogenital, or metabolic disorders, and diseases, particularly kidney rejection, kidney stones, or kidney failure. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal, endocrine, or haemolymphoid system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., kidney, metabolic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:155 as residues: Phe-7 to Asn-12, Thr-18 to Asp-27, Glu-33 to Ile-42, Ser-62 to Asp-80, Gln-84 to Asn-89, Gln-108 to Leu-132, Lys-137 to Ser-156, Ser-163 to Leu-179, Glu-190 to Gln-195, Lys-204 to Lys-212, Ile-219 to Arg-227.

The tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Alternatively, expression within the kidney cortex indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies

directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:59 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 688 of SEQ ID NO:59, b is an integer of 15 to 702, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 50

The translation product of this gene was shown to have homology to the human complexin I and II (See Genbank Accession No. gil2465459) which are part of a family of proteins that compete with alpha-SNAP, but not synaptotagmin, for SNAP receptor binding which are important in vesicular transport within the cell. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

TLHPPQEPQRPEAPDAGDPAPLPSTSSVGSSSGGACGVPCAHWRVCGLI  
HLVALRGGIRAPVSPPFMFNLHHNLLNLR (SEQ ID NO:285), EPQRPEAPDAGD  
PAPLPSTSS (SEQ ID NO:286), and/or RVCGLIHLVALRGGI (SEQ ID NO:287).

Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 4. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 4.

This gene is expressed primarily in adult brain, and to a lesser extent, in kidney cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or renal disorders, particularly depression, Alzheimers, schizophrenia; acute renal failure; or renal dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous, renal, or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, urogenital, renal, or cancerous and

5 wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID

10 NO:156 as residues: Cys-32 to Ser-62, Tyr-86 to Gly-94, Ser-106 to Ala-114.

The tissue distribution in brain combined with its homology to a conserved vesicular transport protein (significant for proper neurotransmitter synthesis and release) indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural

15 disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection

20 of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Alternatively, the tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema,

25 pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets

30 for the above listed tissues. It is also expressed in kidney, suggesting a role in kidney functions such as proximal tubule regeneration or glomerular filtration. Thus it may be useful in the treatment of acute renal failure and or kidney disorders, such as Wilm's tumor.

Many polynucleotide sequences, such as EST sequences, are publicly available

35 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:60 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1081 of SEQ ID NO:60, b is an integer of 15 to 1095, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 51

The translation product of this gene shares sequence homology with Apo E4L1 protease which is thought to be important in catalyzing the formation of abnormal beta/A4 variants of beta-amyloid protein. The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in kidney medulla.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal, urogenital, or metabolic disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, renal, urogenital, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:157 as residues: Trp-17 to Ala-25, Ser-33 to Ser-42.

The tissue distribution in kidney tissue, combined with the homology to the Apo E4L1 indicates the protein product of this gene could be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilm's Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney,

polycystic kidney, and Falconi's syndrome. Alternatively, polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, prevention, and/or treatment of various metabolic disorders which include, but are not limited to, Tay-Sachs disease, phenylketonuria, galactosemia, hyperlipidemias, porphyrias, and Hurler's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:61 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 853 of SEQ ID NO:61, b is an integer of 15 to 867, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.

## 20 FEATURES OF PROTEIN ENCODED BY GENE NO: 52

The translation product of this gene was shown to have homology to the human T-lymphocyte maturation associated protein which is thought to be involved in T-cell specific vesicular trafficking (See Genbank Accession No.P21145).

This gene is expressed primarily in synovial hypoxia, and to a lesser extent in breast lymph node.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive disorders, particularly breast cancer; hematopoietic disorders; immune dysfunction; arthritis, or joint replacement. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., skeletal, developmental, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, amniotic fluid,



urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5           The tissue distribution in lymph nodes, combined with the homology to the conserved T-lymphocyte maturation protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment or diagnosis of immune disorders and related diseases. Likewise, the expression of this gene in breast lymph node indicates a role in hematopoietic cells or immune function, and the gene  
10   product may be involved in immune surveillance, immune modulation, or in the activation or priming of leukocytes. Alternatively, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and  
15   inflammation) in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Protein is useful in the modulation of  
20   the immune response to autoimmune, proliferative, or degenerative cells or tissues, particularly of the skeletal system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

          Many polynucleotide sequences, such as EST sequences, are publicly available  
25   and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:62 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
30   polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1120 of SEQ ID NO:62, b is an integer of 15 to 1134, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 53

The translation product of this gene was shown to have homology to the human E2F-6 protein which is thought to serve as a transcriptional repressor in the establishment of proper cell-cycle regulation (See Genebank Accession No.gil3080767). One embodiment of this gene comprises polypeptides of the following amino acid sequence:

QGYSTKPRLMVPLKMDSITVHIRSTNGPIDVYLCEVEQGQTSNKRSEGVGTSSS  
ESTHPEGPEEEENPQQSEELLEVS (SEQ ID NO:288), DSITVHIRSTNGPIDVYL  
CEVEQGQTSNKR (SEQ ID NO:289), LMVPLKMDSITVHIRSTNGPIDVYL (SEQ  
ID NO:290), and/or QGQTSNKRSEGVGTSSSESTHPEGPE (SEQ ID NO:291). An  
additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in hematopoietic cells and tissues (e.g., T cells; B cell lymphoma; bone marrow), and to a lesser extent, in adrenal gland tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; B cell lymphoma; adrenal gland tumor; Addison's disease; Cushing's syndrome; defects in immune function. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and/or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hematopoietic cells and tissues, combined with the homology to the human E2F-6 protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of hematopoietic disorders and/or disorders of the endocrine system. Elevated levels of expression of this gene in T cells indicates that it may be useful in the modulation of immune function or in immune surveillance, and may influence cytokine production. Likewise, expression in bone marrow indicates that it may play a role in the regulation of hematopoiesis, either

through effects on the proliferation or the differentiation of blood cell lineages, or in the maintenance or expansion of stem cells.

Expression in the adrenal gland or adrenal gland tumor indicates that this gene may play a role in the proliferation of cells within the adrenal gland - and in the proliferation of cells in general. Additionally, expression in the adrenal gland indicates that this may be useful in the treatment and/or diagnosis of disorders of the adrenal gland, including Addison's disease, Cushing's syndrome, and masculinization and/or feminization. It may also exert effects on the secretion of adrenaline and noradrenaline. Moreover, the protein is useful in inhibiting the proliferation of tumor cells and tissues, either directly or indirectly. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:63 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1434 of SEQ ID NO:63, b is an integer of 15 to 1448, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.

## 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 54

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: RPTRPSILGLYVDLYVFCI (SEQ ID NO:292). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 14. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 14.

This gene is expressed primarily in melanocytes, and to a lesser extent in placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, integumentary, developmental, and/or vascular disorders and diseases, particularly skin cancer; vascular leak syndrome; tumors of an endothelial cell origin; tumors of an epidermal cell origin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential

5 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin and/or endothelium, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, developmental, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial

10 fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:160 as residues: Lys-20 to Leu-28.

15 The tissue distribution in melanocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma,

20 malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and

25 xanthelasma. Moreover, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athletes foot, and ringworm).

Alternatively, expression within placental tissue and other cellular sources

30 marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Moreover, the protein is useful in the detection, treatment, and/or prevention of various vascular conditions, which include, but are not limited to vascular leak syndrome, stroke, embolism, aneurysm, atherosclerosis, or microvascular disease. Similarly, embryonic development also involves decisions involving cell differentiation

35 and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein,

as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

- 5 ID NO:64 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of
- 10 a-b, where a is any integer between 1 to 742 of SEQ ID NO:64, b is an integer of 15 to 756, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 55

- The translation product of this gene shares sequence homology with a C. elegans protein which may be important in development (See Genebank Accession No.gil289768). In specific embodiments, polypeptides of the invention comprise the
- 20 following amino acid sequence: CGACTXLSDLSDSRRCGCKGSSLRHTAVA (SEQ ID NO:293). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

- 25 This gene is expressed primarily in cancers, and hematopoietic cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; cancers; prostate cancer; Hodgkin's lymphoma;
- 30 chronic lymphocytic leukemia; bone cancer; disorders of the vasculature. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and circulatory systems, expression of this gene at significantly higher or lower levels may
- 35 be routinely detected in certain tissues or cell types (e.g., hematopoietic, developmental, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell

sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID  
5 NO:161 as residues: Lys-6 to Leu-12, Phe-36 to Pro-45.

The tissue distribution in hematopoietic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders and cancer. This gene product is expressed at elevated levels in a variety of cancers, suggesting that it may be involved in the control or regulation of  
10 aberrant cell proliferation and/or cell transformation. It is also expressed in endothelial cells, suggesting that it may be involved in angiogenesis that supports the development of cancer. Likewise, it is expressed at elevated levels in a variety of hematopoietic tissues, suggesting that it may be involved in the proliferation, survival, and/or differentiation of blood cell lineages. The uses include bone marrow cell ex- vivo  
15 culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the  
20 differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
25 ID NO:65 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
30 a-b, where a is any integer between 1 to 482 of SEQ ID NO:65, b is an integer of 15 to 496, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 56

This gene is expressed primarily in spleen (from patients with chronic lymphocytic leukemia), and to a lesser extent in placenta.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; chronic lymphocytic leukemia; placental insufficiency; disorders of the vasculature; tumors of an endothelial cell origin; aberrant  
10 angiogenesis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, reproductive, and/or circulatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell  
15 types (e.g., reproductive, immune, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

20 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:162 as residues: Ser-18 to Gly-23.

The tissue distribution in spleen and placenta indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders, such as CLL, as well as disorders of the circulatory system  
25 and/or female reproductive system. This gene product is expressed at elevated levels in the spleen - particularly of patients with chronic lymphocytic leukemia - and in the placenta, a highly vascularized tissue suggesting that this gene product may be expressed at higher levels by endothelial cells. These observations suggest that this gene may be involved in the survival, proliferation, and/or differentiation of blood cells,  
30 or may control their activation state or immune function. Likewise, it indicates that this gene product may be involved in endothelial cell function, such as angiogenesis, or may simply be produced by endothelial cells to be released into the circulation and have an effect on cells at scattered sites within the body.

Moreover, the protein is useful in the detection, treatment, and/or prevention of  
35 a variety of vascular disorders and conditions, which include, but are not limited to microvascular disease, vascular leak syndrome, aneurysm, stroke, embolism, thrombosis, and/or atherosclerosis. Protein, as well as, antibodies directed against the

protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:66 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 543 of SEQ ID NO:66, b is an integer of 15 to 557, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 57

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GRPTRPI (SEQ ID NO:294). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T cells and spleen (from a patient with chronic lymphocytic leukemia), and to a lesser extent, in lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; chronic lymphocytic leukemia; inflammation; immune dysfunction; autoimmune disorders; pulmonary disorders, particularly fibrosis; ARDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune or respiratory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, pulmonary, lung, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, pulmonary surfactant or sputum, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.



The tissue distribution in T-cells and lung indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders or disorders of the lung. This gene product is expressed at elevated levels in T cells and the spleen of a patient with CLL, as well as in the lung.

5 Thus, this gene product may play a role in the proliferation, survival and/or differentiation of blood cell lineages, or in the activation and modulation of hematopoietic cells and cell function. Alternately, this protein may be involved in lung function or disorders of the lung, including fibrosis, inflammation, or ARDS. The protein is useful in the modulation of the immune response to proliferative or aberrant  
10 cells or cell types, particularly in the lung. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
15 ID NO:67 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
20 a-b, where a is any integer between 1 to 660 of SEQ ID NO:67, b is an integer of 15 to 674, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.

## 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 58

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

DPRVRDLQQKDIGVKPEFSFNIPRAKRELAQLNKCTSPQQKLVCLRKVVQLITQ  
30 SPSQRVNLET (SEQ ID NO:295), QQKDIGVKPEFSFNIPRAKRE (SEQ ID NO:296), and/or KCTSPQQKLVCLRKVVQLITQSPSQ (SEQ ID NO:297).

Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in myeloid progenitor cells.

Therefore, polynucleotides and polypeptides of the invention are useful as  
35 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic or immune disorders and diseases; leukemias;

inflammation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in myeloid progenitor cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders and immune dysfunction. This gene is expressed at elevated levels in a myeloid progenitor cell line, suggesting that it may be involved in the proliferation, survival, and/or differentiation of hematopoietic cell lineages. In addition, it may be produced by myeloid cells in order to recruit other blood cells to a particular site, such as a site of inflammation, or it may be responsible for activating hematopoietic cells, such as T cells. Similarly, the expression within myeloid progenitor cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:68 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 780 of SEQ ID NO:68, b is an integer of 15 to 794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.

5

## FEATURES OF PROTEIN ENCODED BY GENE NO: 59

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: QK

10 EWKLFLRGRQNEKSGYQKLLELILLDQTVRVVVTAGSAILQKCHFYEVLSEIKRL  
GDHLAEKTSXLPNHSEPDHDTDAGLERTNPEYENEVEASMDMDLLESSNISE  
GEIERLINLLEEVFHLMETAPHTMIQQPVKSFT (SEQ ID NO:298), LRGRQNEK  
SGYQKLLELILLDQTVRVV (SEQ ID NO:299), ILQKCHFYEVLSEIKRLGDHLAE  
KTS (SEQ ID NO:300), DAGLERTNPEYENEVEASMDMD (SEQ ID NO:301),  
15 and/or NISEGEIERLINLLEEVFHLMETAPH (SEQ ID NO:302). Polynucleotides  
encoding these polypeptides are also encompassed by the invention. The gene encoding  
the disclosed cDNA is believed to reside on chromosome 8. Accordingly,  
polynucleotides related to this invention are useful as a marker in linkage analysis for  
chromosome 8.

20 This gene is expressed primarily in infant and fetal brain, and to a lesser extent,  
in hematopoietic tissues, such as T cells, B cell lymphoma, and bone marrow cell lines.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are  
25 not limited to, hematopoietic disorders; lymphoproliferative disorders; neurological  
disorders such as Alzheimers and schizophrenia, in addition to developmental disorders  
and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are  
useful in providing immunological probes for differential identification of the tissue(s)  
or cell type(s). For a number of disorders of the above tissues or cells, particularly of  
30 the immune system and/or CNS, expression of this gene at significantly higher or lower  
levels may be routinely detected in certain tissues or cell types (e.g., neural, immune,  
developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,  
serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue  
or cell sample taken from an individual having such a disorder, relative to the standard  
35 gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:165 as residues: Pro-7 to Tyr-14.

The tissue distribution in infant and fetal brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of neurodegenerative disorders and/or hematopoietic disorders. This gene displays elevated levels of expression in fetal/infant brain, as well as in a variety of hematopoietic tissues. Thus, this gene product may play a role in the development of the brain and/or nervous system, and may be involved in the survival or differentiation of neurons. It may therefore be useful in the treatment of neurological disorders such as Alzheimers, schizophrenia, or ALS, and may protect neurons or effect neuronal regeneration. Likewise, this gene product may play a role in hematopoietic development, and could be useful in their proliferation, survival, and/or differentiation of blood cell lineages.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/ immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumors); hemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures.

The protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain neurodegenerative disorders, such as spinal muscular atrophy (SMA). Therefore, the polynucleotides and polypeptides of the present invention are useful in

treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:69 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1901 of SEQ ID NO:69, b is an integer of 15 to 1915, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 60

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: RRTSGSPXAAGIRHEGGFI (SEQ ID NO:303).

Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in macrophages, and to a lesser extent, in bone marrow cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; susceptibility to infection; leukemias; immune dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the

expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:166 as residues: Met-1 to Asn-7, Leu-18 to Gly-24.

5           The tissue distribution in macrophages and bone marrow cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders. This gene is expressed at higher levels in hematopoietic cells such as macrophages, as well as in tissues that support hematopoietic development, such as bone marrow stromal cells. Thus, this gene  
10       product may effect hematopoietic cell proliferation, survival, and/or differentiation, as well as hematopoietic cell activation and immune function. Thus, this gene may be useful in boosting stem cell numbers, enhancing immune surveillance, or combatting leukemias or lymphoproliferative disorders.

          The uses include bone marrow cell ex vivo culture, bone marrow  
15       transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation  
20       and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

          Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
25       ID NO:70 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
30       a-b, where a is any integer between 1 to 719 of SEQ ID NO:70, b is an integer of 15 to 733, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 61

The translation product of this gene shares sequence homology with carboxyamido-triazole resistance proteins which are thought to be important in resistance to treatment of cancer with carboxyamido-triazole (CAI) (See Genbank Accession No.R77365). Moreover, the protein product of this gene shares homology with the human silencer of death domains protein (See Genbank Accession No.gil4160014 (AF111116)). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: MNRHNFPCSVHQYESSGTVNDD  
 5 SDLLDSQVQYSAEPQLYGNATSDHPNNQDQSSSLPEECVPSDESTPPSIKKIIHV  
 10 LEKVQYLEQEVEEFVGGKTKDKAYWLLEMLTKELLEDSVETGGQDSVRQARK  
 EAVCKIQAILKKKKKN S (SEQ ID NO:304), GARATAPVTVRPTAATTGLGVE  
 MCRYTHLHPYILFALNLPSPFPGGCAGAARRRPPGWEKAEEAMATIPREA  
 PGQSLVEPEEATRV (SEQ ID NO:305), PVTVRPTAATTGLGVEMCRYTHLHP  
 15 (SEQ ID NO:306), PYILFALNLPSPFPGGCAGAARRR (SEQ ID NO:307),  
 KAEEAMATIPREAPGQSLVE (SEQ ID NO:308), MNRHNFPCSVHQYESSGTV  
 NNDDSDL (SEQ ID NO:309), DSQVQYSAEPQLYGNATSDHPNNQ (SEQ ID  
 NO:310), HPNNQDQSSSLPEECVPSDESTPPS (SEQ ID NO:311), EVEEFVGGK  
 KTDKAYWLLEMLTKE (SEQ ID NO:312), and/or LE LDSVETGGQDSVRQARK  
 20 EAVCK (SEQ ID NO:313). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

Numerous biological actions, for instance, response to certain stimuli and  
 25 natural biological processes, are controlled by factors, such as cytokines. Many cytokines act through receptors by engaging the receptor and producing an intra-cellular response. For example, tumor necrosis factors (TNF) alpha and beta are cytokines, which act through TNF receptors to regulate numerous biological processes, including protection against infection and induction of shock and inflammatory disease. The TNF  
 30 molecules belong to the "TNF-ligand" superfamily, and act together with their receptors or counter-ligands, the "TNF-receptor" superfamily.

So far, nine members of the TNF ligand superfamily have been identified and ten members of the TNF-receptor superfamily have been characterized. Among the  
 35 ligands, there are included TNF-a, lymphotoxin-a (LT- a, also known as TNF-b), LT-b (found in complex heterotrimer LT-a2-b), FasL, CD40L, CD27L, CD30L, 4-1BBL, OX40L and nerve growth factor (NGF). The superfamily of TNF receptors includes the p55TNF receptor, p75TNF receptor, TNF receptor-related protein, FAS antigen or

APO-1, CD40, CD27, CD30, 4-1BB, OX40, low affinity p75 and NGF-receptor (Meager, A., *Biologicals*, 22:291-295 (1994)).

Many members of the TNF-ligand superfamily are expressed by activated T-cells, implying that they are necessary for T-cell interactions with other cell types which underlie cell ontogeny and functions. (Meager, A., *supra*). Considerable insight into the essential functions of several members of the TNF receptor family has been gained from the identification and creation of mutants that abolish the expression of these proteins. For example, naturally occurring mutations in the FAS antigen and its ligand cause lymphoproliferative disease (Watanabe-Fukunaga, R., et al., *Nature* 356:314 (1992)), perhaps reflecting a failure of programmed cell death. Mutations of the CD40 ligand cause an X-linked immunodeficiency state characterized by high levels of immunoglobulin M and low levels of immunoglobulin G in plasma, indicating faulty T-cell-dependent B-cell activation (Allen, R.C. et al., *Science* 259:990 (1993)).

Targeted mutations of the low affinity nerve growth factor receptor cause a disorder characterized by faulty sensory innervation of peripheral structures (Lee, K.F. et al., *Cell* 69:737 (1992)). TNF and LT-a are capable of binding to two TNF receptors (the 55- and 75-kd TNF receptors). A large number of biological effects elicited by TNF and LT-a, acting through their receptors, include hemorrhagic necrosis of transplanted tumors, cytotoxicity, a role in endotoxic shock, inflammation, immunoregulation, proliferation and anti-viral responses, as well as protection against the deleterious effects of ionizing radiation. TNF and LT-a are involved in the pathogenesis of a wide range of diseases, including endotoxic shock, cerebral malaria, tumors, autoimmune disease, AIDS and graft-host rejection (Beutler, B. and Von Huffel, C., *Science* 264:667-668 (1994)).

Mutations in the p55 Receptor cause increased susceptibility to microbial infection. Moreover, an about 80 amino acid domain near the C-terminus of TNFR1 (p55) and Fas was reported as the "death domain," which is responsible for transducing signals for programmed cell death (Tartaglia et al., *Cell* 74:845 (1993)). Apoptosis, or programmed cell death, is a physiologic process essential for the normal development and homeostasis of multicellular organisms (H. Steller, *Science* 267:1445-1449 (1995)). Derangements of apoptosis contribute to the pathogenesis of several human diseases including cancer, neurodegenerative disorders, and acquired immune deficiency syndrome (C.B. Thompson, *Science* 267:1456-1462 (1995)).

Recently, much attention has focused on the signal transduction and biological function of two cell surface death receptors, Fas/APO-1 and TNFR-1 (J.L. Cleveland et al., *Cell* 81:479-482 (1995); A. Fraser, et al., *Cell* 85:781-784 (1996); S. Nagata et al., *Science* 267:1449-56 (1995)). Both are members of the TNF receptor family which



also include TNFR-2, low affinity NGFR, CD40, and CD30, among others (C.A. Smith et al., *Science* 248:1019-23 (1990); M. Tewari et al., in *Modular Texts in Molecular and Cell Biology* M. Purton, Heldin, Carl, Ed. (Chapman and Hall, London, 1995).

5 While family members are defined by the presence of cysteine-rich repeats in their extracellular domains, Fas/APO-1 and TNFR-1 also share a region of intracellular homology, appropriately designated the "death domain", which is distantly related to the *Drosophila* suicide gene, reaper (P. Golstein, et al., *Cell* 81:185-186 (1995); K. White et al., *Science* 264:677-83 (1994)). This shared death domain indicates that both  
10 receptors interact with a related set of signal transducing molecules that, until recently, remained unidentified. Activation of Fas/APO-1 recruits the death domain-containing adapter molecule FADD/MORT1 (A.M. Chinnaiyan et al., *Cell* 81: 505-12 (1995); M. P. Boldin et al., *J. Biol Chem* 270:7795-8 (1995); F.C. Kischkel et al., *EMBO* 14:5579-5588 (1995)), which in turn binds and presumably activates FLICE/MACH1,  
15 a member of the ICE/CED-3 family of pro-apoptotic proteases (M. Muzio et al., *Cell* 85:817-827 (1996); M.P. Boldin et al., *Cell* 85:803-815 (1996)).

While the central role of Fas/APO-1 is to trigger cell death, TNFR-1 can signal an array of diverse biological activities-many of which stem from its ability to activate NF-kB (L.A. Tartaglia et al., *Immunol Today* 13:151-3 (1992)). Accordingly, TNFR-1  
20 recruits the multivalent adapter molecule TRADD, which like FADD, also contains a death domain (H. Hsu et al., *Cell* 81:495-504 (1995); H. Hsu, et al., *Cell* 84:299-308 (1996)). Through its associations with a number of signaling molecules including FADD, TRAF2, and RIP, TRADD can signal both apoptosis and NF-kB activation (H. Hsu et al., *Cell* 84:299-308 (1996); H. Hsu, et al., *Immunity* 4:387-396 (1996)).

25 Recently, a new apoptosis -inducing TNF ligand has been discovered. S.R. Wiley et al. (*Immunity* 3:673-682 (1995)) named the molecule - iTNF-related apoptosis-inducing ligand or simply iTRAIL. The molecule was also called iApo-2 ligand or iApo-2L. R.M. Pitt et al., *J. Biol. Chem.* 271:12687-12690 (1996). This molecule was also disclosed in co-pending U.S. provisional application no.  
30 60/013,405. For convenience, the molecule will be referred to herein as TRAIL. Unlike FAS ligand, whose transcripts appear to be largely restricted to stimulated T-cells, significant levels of TRAIL are detected in many human tissues (e.g., spleen, lung, prostate, thymus, ovary, small intestine, colon, peripheral blood lymphocytes, placenta, kidney), and is constitutively transcribed by some cell lines.

35 It has been shown that TRAIL acts independently from the Fas ligand (Wiley et al., *supra*). It has also been shown that TRAIL activates apoptosis rapidly, within a time frame that is similar to death signaling by Fas/Apo-1L, but much faster than TNF-

induced apoptosis. S.A. Marsters et al., *Current Biology* 6:750-752 (1996). The inability of TRAIL to bind TNFR-1, Fas, or the recently identified DR3, indicates that TRAIL may interact with a unique receptor(s). Several unique receptors for TRAIL have already been identified. In co-pending U.S. provisional patent application no. 60/035,722, DR4, a novel death domain containing receptor for TRAIL, was disclosed. See, Pan et al., *Science* 276,111-113 (April 1997). The TR5 receptor, the subject of co-pending U.S. provisional patent application 60/035,496, has now been shown to bind TRAIL. In co-pending U.S. provisional patent application no. 60/xxxxxx, it was predicted that the TR10 receptor would also bind TRAIL, owing to sequence homology with DR4.

The effects of TNF family ligands and TNF family receptors are varied and influence numerous functions, both normal and abnormal, in the biological processes of the mammalian system. There is a clear need, therefore, for identification and characterization of such receptors and ligands that influence biological activity, both normally and in disease states. In particular, there is a need to isolate and characterize additional novel receptors that bind to or antagonize TRAIL.

This gene is expressed primarily in fetal liver, and to a lesser extent in activated neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer; hematopoietic, developmental, and hepatic disorders and disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly for the immune system and for cancers such as melanomas and ovarian cancers, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., bile, lymph, serum, plasma, amniotic fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:167 as residues: Arg-5 to Tyr-21, Arg-40 to Pro-46, Glu-65 to Gly-77, Pro-80 to Gly-109.

The tissue distribution in fetal liver and neutrophils, combined with the homology to the silencer of death domain and CAI resistance proteins indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection, treatment, and/or prevention of cancers, particularly those resistant to the anti-cancer compound, carboxyamido-triazole. Likewise, elevated expression in fetal liver and neutrophils indicates a potential role in the proliferation, survival, and/or differentiation of hematopoietic lineages.

Similarly, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g., hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). In addition the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various wound-healing models and/or tissue trauma.

Moreover, the expression within fetal tissue and other cellular sources marked by proliferating cells indicates this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain neurodegenerative disorders, such as spinal muscular atrophy (SMA). Therefore, the polynucleotides and polypeptides of the present invention are useful in treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions.

Thus this protein may also be involved in the modulation of apoptosis or tissue differentiation and could again be useful in cancer therapy. The protein may be beneficial in protecting cells or tissues from initiating the pathway to apoptosis, which would provide tremendous therapeutic benefit to degenerative conditions, particularly in the developing embryo and diseased tissues and cells, and in autoimmune diseases, for example. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:71 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1252 of SEQ ID NO:71, b is an integer of 15 to 1266, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 62

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: IRHEYPVLIQFSVSYRKSFIFCLPE (SEQ ID NO:314). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory and immune or hematopoietic diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of inflammatory diseases such as rheumatoid arthritis, psoriasis, inflammatory bowel disease, sepsis and autoimmune disorders. In addition, it may also represent a secreted factor that influences the differentiation or behavior of other blood cells, or that recruits hematopoietic cells to sites of injury. Similarly, the tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages.

The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

10. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:72 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.
- 15 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 471 of SEQ ID NO:72, b is an integer of 15 to 485, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.

20

## **FEATURES OF PROTEIN ENCODED BY GENE NO: 63**

This gene is expressed primarily in neutrophils.

- 25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders and diseases, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these
- 30 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,
- 35 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:73 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 625 of SEQ ID NO:73, b is an integer of 15 to 639, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 64

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, immune or hematopoietic disorders and diseases, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:170 as residues: Ala-14 to Lys-19, Gln-67 to Trp-79, Pro-100 to Pro-110, Thr-126 to Arg-132.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:74 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 518 of SEQ ID NO:74, b is an integer of 15 to 532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.

5

## FEATURES OF PROTEIN ENCODED BY GENE NO: 65

The translation product of this gene was shown to have homology to the human diaphanous protein which is thought to regulate cytokinesis in meiosis and mitosis within various cell types and would likely be useful for regulating cellular division, particularly in treating cancer or other disorders involving proliferating cells or tissues (See Genebank Accession No. P48608). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

15 ADVELVDPXGCRNSARAPARKKEWSAWPRIRVIRARESLGS (SEQ ID NO:315). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

20 This gene is expressed primarily in dendritic cells, and to a lesser extent, in IL-4 induced endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders and diseases, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, endothelial, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

35

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:171 as residues: Tyr-32 to Ala-39.



The tissue distribution in dendritic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the homology to a cell-cycle regulatory protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:75 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 500 of SEQ ID NO:75, b is an integer of 15 to 514, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 66

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 5 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 not limited to, immune or hematopoietic disorders and diseases, particularly  
 inflammatory disorders. Similarly, polypeptides and antibodies directed to these  
 polypeptides are useful in providing immunological probes for differential identification  
 10 of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,  
 particularly of the immune system, expression of this gene at significantly higher or  
 lower levels may be routinely detected in certain tissues or cell types (e.g., immune,  
 hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,  
 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample  
 15 taken from an individual having such a disorder, relative to the standard gene  
 expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
 individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID  
 NO:172 as residues: Ser-46 to Lys-55, Ser-67 to Pro-75.

20 The tissue distribution in neutrophils indicates that polynucleotides and  
 polypeptides corresponding to this gene are useful for the diagnosis and treatment of a  
 variety of immune system disorders. Expression of this gene product indicates a role in  
 regulating the proliferation; survival; differentiation; and/or activation of potentially all  
 hematopoietic cell lineages, including blood stem cells. This gene product may be  
 25 involved in the regulation of cytokine production, antigen presentation, or other  
 processes that may also suggest a usefulness in the treatment of cancer (e.g., by  
 boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product  
 may be involved in immune functions. Therefore it may be also used as an agent for  
 30 immunological disorders including arthritis, asthma, immune deficiency diseases such  
 as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and  
 psoriasis. and tissues. In addition, this gene product may have commercial utility in the  
 expansion of stem cells and committed progenitors of various blood lineages, and in the  
 differentiation and/or proliferation of various cell types. Protein, as well as, antibodies  
 35 directed against the protein may show utility as a tumor marker and/or immunotherapy  
 targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:76 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 630 of SEQ ID NO:76, b is an integer of 15 to 644, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 67

This gene is expressed primarily in thymus and neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; T cell lymphoma; inflammatory and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, amniotic fluid, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:173 as residues: Cys-24 to Asn-31.

The tissue distribution in thymus and neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of inflammatory and immune disorders, particularly rheumatoid arthritis, sepsis, psoriasis, inflammatory bowel disorder, and autoimmune diseases such as lupus. Likewise, its expression in thymus and neutrophils indicates that it may play a more general role in immune function, immune surveillance, or in the activation

or priming of immune cells, such as T cells. It may also be involved in the proliferation, survival, and/or differentiation of blood cell lineages - for example, in the microenvironment of the thymic stroma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:77 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1185 of SEQ ID NO:77, b is an integer of 15 to 1199, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 68**

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates myeloid cells, or more generally, immune or hematopoietic cells, in addition to other cells or cell-types through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the JAK-STAT pathway. The JAK-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the JAK-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: EFGTSRGPVPLSSTSPMPSRLVIRAHSLLF (SEQ ID NO:316). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic diseases and disorders, particularly

inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:174 as residues: Glu-60 to Lys-66.

The tissue distribution in neutrophils, combined with the detected GAS biological activity, indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of inflammatory and immune disorders, particularly rheumatoid arthritis, sepsis, psoriasis, inflammatory bowel disorder, and auto immune diseases such as lupus. Likewise, it may also be involved in influencing the activation of other blood cell lineages, or in the recruitment of hematopoietic cells to specific sites, such as sites of injury or inflammation.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumors); hemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:78 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 646 of SEQ ID NO:78, b is an integer of 15 to 660, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 69

The translation product of this gene was shown to have homology to catalase (hydrogen-peroxide:hydrogen-peroxide oxidoreductase) which is known to be involved in the elimination of hydrogen peroxide produced during cellular metabolism. (See Genebank Accession No.gil984737). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

FRAWRNHGHSCFLCEIVIRSQFHTTYEPEA (SEQ ID NO:317), ADNFTQETAM  
 TMITPSSKLTLTKGNKWSSTAVAALELVDPGCRNSARAVLLIWGHGSSGK  
 MALCGVEVSPRVGGSVPVHRYLLAAHIHSEALLSQLRM (SEQ ID NO:318), TA  
 MTMITPSSKLTLTKGNKWSST (SEQ ID NO:319), SSGKMALCGVEVSPRVGG  
 SVPVHRYL (SEQ ID NO:320), and/or VDPVKGG (SEQ ID NO:321).

Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory, immune, or metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain

tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:175 as residues: Thr-36 to Pro-47, Pro-71 to Ser-77, Asn-117 to Lys-127.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the homology to catalase indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, detection, treatment, and/or prevention of a variety of metabolic disorders. As elevated levels of peroxide in cells and tissues leads to oxidative damage, largely through the generation of oxide free-radicals, mutations within the catalase gene may lead to the accumulation of cellular mutations over time and could predispose an individual to cancer or other disorder and disease. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:79 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 510 of SEQ ID NO:79, b is an integer of 15 to 524, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 70

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: IRHERHELVPNSARDF (SEQ ID NO:322). Polynucleotides  
10 encoding these polypeptides are also encompassed by the invention

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
15 not limited to, immune or hematopoietic disorders and diseases, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or  
20 lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
25 individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or  
30 activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product  
35 may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and



psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:80 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 420 of SEQ ID NO:80, b is an integer of 15 to 434, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 71

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ATSHCG (SEQ ID NO:323). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders and diseases, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:81 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 721 of SEQ ID NO:81, b is an integer of 15 to 735, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.

## 30 FEATURES OF PROTEIN ENCODED BY GENE NO: 72

This gene has homology with galectin, and is a new member of the family of beta-galactoside binding protein, similar to the galaptin (S-lectin) family. Recently, it has been shown that galactin induced apoptosis of T cells and T cell leukaemia cell lines. It is believed that galactins function in growth regulation, immunomodulatory activity, cell-cell and cell-substrate interactions, and induce apoptosis of T cells. Likewise, it is proposed that the translation product of this gene is useful for the study,

treatment, detection, and/or prevention of a variety of immune diseases, particularly autoimmune disease, cancer, and inflammatory disease. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

AHGQIEGKALTHDHTAEKWQRQDLNLEPLAPHTSNLNHSPYNTTYVVK (SEQ

5 ID NO:324). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
10 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic or hematopoietic disorders; fibrosis; inflammation and immune response. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,  
15 particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene  
20 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the  
25 protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

30 Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. and tissues. In addition, this gene product may have commercial utility in the  
35 expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell

5 proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/ immunosuppressant activities (e.g., for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g., for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g., for treating  
10 wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g., for treating infections, tumors); hemostatic or thrombolytic activity (e.g., for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g., for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation  
15 of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available  
20 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:82 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 708 of SEQ ID NO:82, b is an integer of 15 to 722, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to a + 14.

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## **FEATURES OF PROTEIN ENCODED BY GENE NO: 73**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LNSSDCQLA (SEQ ID NO:325). Polynucleotides encoding  
35 these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic or immune disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:179 as residues: Glu-21 to Thr-26.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:83 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 771 of SEQ ID NO:83, b is an integer of 15 to 785, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to a + 14.

## 10 FEATURES OF PROTEIN ENCODED BY GENE NO: 74

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and/or hemopoietic disorders and diseases, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:180 as residues: Gly-11 to Gly-43.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein is useful in modulating the immune response to proliferative cells and tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:84 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 556 of SEQ ID NO:84, b is an integer of 15 to 570, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to a + 14.

## 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 75

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: TPHNLSARRLSGTMYGFFALQLTVLLVHYFFLI (SEQ ID NO:326). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological or hematopoietic disorders, particularly inflammatory conditions, and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types

- (e.g., hematopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

- Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

- Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:85 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 891 of SEQ ID NO:85, b is an integer of 15 to 905, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.



## FEATURES OF PROTEIN ENCODED BY GENE NO: 76

5 This gene was shown to have homology to the human IL-15 gene which is known to be play an integral role in immune modulation (See Genebank Accession No. gb|X91233|HSDNAIL15). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

NSARAKMRLSTNLCIILINILIQNVLFNFRKIIFKFLPCA (SEQ ID NO:327).

10 Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological or hematopoietic disorders, particularly inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:182 as residues: Gln-24 to Ser-31.

The tissue distribution in neutrophils combined with the homology to a conserved immune chemokine indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune

functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:86 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 692 of SEQ ID NO:86, b is an integer of 15 to 706, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 77

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ISLCKRSG @. Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in melanocyte, activated monocyte, spleen and osteosarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, integumentary, and/or skeletal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and

skeletal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, skeletal, integumentary, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:183 as residues: Val-33 to Gly-42, Val-52 to Thr-57, Glu-65 to Leu-72.

The tissue distribution in activated monocyte and spleen tissues and cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. The expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Alternatively, the expression in melanocyte tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. Moreover, such disorders may predispose increased

susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athlete's foot, and ringworm). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:87 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1530 of SEQ ID NO:87, b is an integer of 15 to 1544, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 78

This gene is expressed primarily in lung, ovary, spinal cord, and hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular, reproductive, neural, or hematopoietic diseases or disorders, particularly ARDS, fibrosis, polycystic disease, spina bifida, and soft-tissue cancers, for example. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., pulmonary, reproductive, skeletal, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., pulmonary surfactant, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:184 as residues: Ser-6 to Ser-11, Lys-28 to Ser-39.

The tissue distribution in spinal cord tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Alternatively, expression in lung tissue may suggest that the translation product of this gene may be useful for the detection, treatment, and/or prevention of various disorders afflicting the cardiovascular system, particularly lung cancer, emphasema, tracheitis, croup, bronchitis, bronchiolitis, allergies, alveolitis, or cancer. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:88 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 826 of SEQ ID NO:88, b is an integer of 15 to 840, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 79

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: NXWIPRAAGIRHXAALGQAGT (SEQ ID NO:328), LLFHMK LRKEVERTGLVLWALLAGAPPPTAGLQLQGSEAISEKVGSGAEGSRGQVPGQL LQQAQQAFLCPQVIHGLLYHLLHDI (SEQ ID NO:329), RKEVERTGLVLWALL AGAPPPTAGL (SEQ ID NO:330), and/or GSRGQVPGQLLQQAQQAFLCPQ

(SEQ ID NO:331). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 10. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 10.

5 This gene is expressed primarily in chronic synovitis, epididymus, and fetal kidney.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal, reproductive, renal, inflammatory, and developmental diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and developing tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, skeletal, renal, inflammatory, pulmonary, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, pulmonary surfactant or sputum, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:185 as residues: Pro-25 to Gln-35.

The tissue distribution in chronic synovitis suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation) in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid.

Alternatively, expression in fetal kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital

kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:89 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 496 of SEQ ID NO:89, b is an integer of 15 to 510, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 80**

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GSRRHVVVGKPGTPCRYRAGIPXVDPRVRSITVIVKMWFLRVVATYGGVER (SEQ ID NO:332). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in infant brain and ovary.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or reproductive disorders and diseases, particularly ovarian cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, reproductive, or cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,

the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in infant brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. In addition the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various wound-healing models and/or tissue trauma. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain neurodegenerative disorders, such as spinal muscular atrophy (SMA).

Therefore, the polynucleotides and polypeptides of the present invention are useful in treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein is useful in the detection, treatment, and/or prevention of reproductive disorders, which include, but are not limited to polycystic disease, infertility, and related endocrine disorders and conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:90 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more



polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 724 of SEQ ID NO:90, b is an integer of 15 to 738, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 81

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: IFSCDSIAIIQIKHLAFP (SEQ ID NO:333). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancer, and other reproductive disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, prostate, and cancerous and wounded tissues) or bodily fluids (e.g., seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:187 as residues: Pro-25 to Pro-30.

The tissue distribution in prostate tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders, particularly prostate cancer and disorders and conditions afflicting the male reproductive system. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:91 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 492 of SEQ ID NO:91, b is an integer of 15 to 506, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 82

The translation product of this gene was found to have homology to the conserved human nitrilase homolog 1 (See Genbank Accession No. gil3242978 (AF069984)) which is thought to play the role of a tumor suppressor, and may be useful in the modulation of cellular proliferation (See, for example, Proc Natl Acad Sci U S A 1998 Jul 21;95(15):8744-9, which is hereby incorporated by reference herein). Such activities are known in the art and described elsewhere herein. Moreover, the translation product of this gene was shown to have homology to the conserved *Saccharomyces cerevisiae* protein YJL126w which is thought to be important in the decarbamylation of N-carbamoyl-D-alpha aminoacids (See Genebank Accession No.gil1008324). In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:  
GLWLSLGGFHERGQDWEQTQKIYNCHVLLNRKGQ (SEQ ID NO:334), AWPRL  
GADSENQLSRAAEQKGAVVATYRKTHLCDVEIPGQGLCVKATLPCLGPVLSH  
LSAHQQARLV (SEQ ID NO:335), RAAEQKGAVVATYRKTHLCDVEIPGQG (SEQ  
ID NO:336), and/or RRDSRAGA (SEQ ID NO:337). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in fetal heart, brain, emangiopericytoma, human adrenal gland tumor, and B cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, neural, immune or hematopoietic disorders and diseases, particularly emangiopericytoma, adrenal gland tumor, B cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a

number of disorders of the above tissues or cells, particularly of the immune, heart, brain, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, developing, reproductive, neural, endocrine, or cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:188 as residues: Cys-2 to Pro-9, His-89 to Gly-96.

The tissue distribution in B cell lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells.

This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Alternatively, expression in the brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, soft-tissue cancers, or disorders of the cardiovascular system. The protein is also useful for the detection, treatment, and/or prevention of endocrine and metabolic disorders, particularly lethargy.

Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:92 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1189 of SEQ ID NO:92, b is an integer of 15 to 1203, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 83

When tested against PC12 cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) pathway. Thus, it is likely that this gene activates sensory neuron cells, or more generally, neural cells and tissues, in addition to other cells or cell-types, through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from JAK-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LSAGNHDT (SEQ ID NO:338). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders and diseases, particularly immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,

serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5           The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product combined with its observed utility as an activator for the early growth response promoter (EGR1) indicates the protein may play a role in regulating the proliferation; survival; differentiation; and/or  
10   activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses).

          Since the gene is expressed in cells of lymphoid origin, the natural gene product  
15   may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.  
20   In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

25           Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:93 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.  
30   Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 696 of SEQ ID NO:93, b is an integer of 15 to 710, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.